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Increasing T-regulatory cells after alemtuzumab or cladribine treatment in people with multiple sclerosis

Submission date
10/10/2022

Recruitment status
No longer recruiting

Registration date
31/10/2022

Overall study status
Completed

Last Edited
18/09/2025

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
Multiple sclerosis (MS) is an autoimmune disease in which the patient's own immune system attacks their brain and spinal cord causing damage and disability. Alemtuzumab and cladribine are licensed treatments for MS that work by depleting immune cells, including the MS-causing cells. The immune system is then allowed to grow back. These treatments are known as induction therapies as there is no need for continuous medication.
Alongside MS-causing cells, both alemtuzumab and cladribine deplete T-regulatory cells (Tregs). Tregs are very important immune cells, as they help keep the rest of the immune system under control, preventing autoimmunity.

The purpose of this study is to test whether low doses of a drug called Proleukin can selectively expand the number of Tregs in people with MS who have been treated with alemtuzumab or cladribine as part of their routine medical care. Increasing Treg levels after alemtuzumab could improve its safety, as 4 out of 10 patients develop a new autoimmune disease (mainly affecting the thyroid gland) after treatment. Increasing Tregs after cladribine could improve its efficacy as 1 in 4 patients get more MS attacks after treatment. Proleukin is the drug version of a naturally occurring immune cell growth factor called interleukin-2 (IL-2). When given at very low doses, IL-2 has been shown to selectively increase Treg numbers in humans in a variety of settings other than MS (such as diabetes, lupus, and vasculitis). It has been shown to be very safe.

Who can participate?
People who have already been treated with alemtuzumab or cladribine for MS

What does the study involve?
In this study, participants will be given 6 subcutaneous injections (i.e. injections under the skin) of low-dose IL-2 over a 3-week period, and provide blood samples to measure T-reg cells.

What are the possible benefits and risks of participating?
We do not expect any clinical benefits over this very short time frame. This is purely a mechanistic study, the readout of which will be Treg frequency before and after treatment.

The main risk of taking part is mild injection site reactions. We do not anticipate any other significant risks as studies in other (non-MS) autoimmune conditions have shown Proleukin at low doses is typically very safe and well tolerated, with few and mild side effects. There is a theoretical risk of increasing cells other than T-regs with Proleukin. However, such an effect, if it occurred, is expected to be short-lived (because the treatment period is very short). Therefore, we would not expect it to pose a significant risk, but we will carefully monitor participants for 4 weeks after stopping treatment (i.e. longer than the treatment period itself).

Where is the study run from?
The University of Cambridge, Department of Clinical Neurosciences (UK)

When is the study starting and how long is it expected to run for?
June 2021 to December 2023

Who is funding the study?
Wellcome Trust (UK)

Who is the main contact?
Dr Joanne Jones (UK)
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Contact information

Type(s)
Principal investigator

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
300567

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
IRAS 300567, CPMS 51189

Study information

Scientific Title
Low-dose interleukin-2 for Treg expansion after induction therapies in multiple sclerosis (LITMUS)

Acronym
LITMUS

Study objectives
Low-dose interleukin-2 can increase the levels of T-regulatory cells (Tregs) in the blood of people with multiple sclerosis who have received treatment with either alemtuzumab or cladribine.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 0712/2021, Wales Research Ethics Committee 7 Carmarthen (Health and Care Research Wales, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, Wales; +44 (0) 2920 230457, (0)7920 565664; Wales.REC7@wales.nhs.uk), ref: 21/WA/0378

Study design
Mechanistic (non-CTIMP) interventional open-label single-centre study

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Immune system recovery (reconstitution) after lymphocyte-depleting therapies in multiple sclerosis

Interventions
All participants will receive 6 ultra-low dose interleukin-2 (Proleukin) subcutaneous injections over the course of 3 weeks. Dose is 0.3 x 10^6 IU/m2, i.e. individual and based on body surface area. Injections will be self-administered.

Intervention Type
Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)
Proleukin

Primary outcome(s)
Change in the frequency of T-regulatory cells in blood after interleukin-2 treatment in participants who have previously received alemtuzumab, measured using flow cytometry; the change in frequency is calculated between baseline (pre-intervention) and after completing the intervention (2-4 days after final interleukin-2 dose)

Key secondary outcome(s))
There are no planned secondary outcomes.
All additional outcomes are exploratory, and can include, but are not limited to:
1. Phenotypic changes e.g. (naïve:memory T-effector ratio, NK cell frequency; T-reg deep immunophenotyping) of lymphocytes in blood measured using flow cytometry at baseline (pre-intervention) and 2-4 days after the final interleukin-2 dose
2. Change in the frequency of T-regulatory cells after interleukin-2 in the blood of participants who had previously received cladribine, measured using flow cytometry at baseline (pre-intervention) and 2-4 days after the final interleukin-2 dose

Completion date
01/12/2023

Eligibility

Key inclusion criteria
1. Able to provide informed consent
2. Definite diagnosis of relapsing-remitting multiple sclerosis
3. Treated with alemtuzumab or cladribine within a specified period before recruitment

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Concurrent treatment with Copaxone, beta interferon, dimethyl fumarate, teriflunomide, fingolimod, natalizumab or ocrelizumab
2. Concurrent use of any other immunosuppressant or cytotoxic therapy
3. Oral/IV high-dose steroid use within 4 weeks of recruitment to the study
4. Participants who have received an investigational drug (including investigational vaccines) or used an invasive investigational medical device within 4 weeks before the screening assessment,

or are currently enrolled in an interventional investigational trial
5. Any planned vaccination in the 4 weeks preceding screening, or at any point during the study
6. Hypersensitivity to Proleukin or any of its excipients
7. History of severe cardiac disease
8. History of malignancy 5 years prior to screening (except adequately treated cervical carcinoma in situ, or basal and squamous cell skin carcinoma)
9. Clinically significant renal, hepatic, or haematological abnormalities as defined in the study protocol
10. Evidence of an active infection. Participants may be recruited a minimum of 48 hours after the resolution of illness or completion of antibacterial/antiviral therapy
11. Pregnant or breastfeeding women; or male and female participants who do not agree to use a highly effective method of contraception during the study
12. Any other factor deemed potentially relevant by the research team

Date of first enrolment
25/01/2022

Date of final enrolment
01/06/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Research council

Funder Name
Wellcome Trust

Alternative Name(s)
Wellcome, WT

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 1		18/09/2025	No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	version 1.3	22/08/2022	25/10/2022	No	Yes
Participant information sheet	version 1.3	22/08/2022	25/10/2022	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes